pts) for 6 months. Rest forced expiratory volume (FEV_1), vital capacity (VC), total lung capacity (TLC), carbon monoxide diffusing capacity (DLco), its alveolar-capillary membrane component (D_M), pulmonary venous and transmitral flow velocities (for monitoring changes in LV end-diastolic pressure, EDP), left ventricular end-diastolic (EDD) and end-systolic (ESD) dimensions, stroke volume (SV), ejection fraction (EF), fiber shortening velocity (Vcf) were measured at baseline, 3 and 6 months. pVO_2, peak dead space to tidal volume ratio (pVD/VT), ventilatory equivalent for CO_2 production (VE/VCO_2), VO_2 at anaerobic threshold (VO_2at) were also determined.

Results: Compared with 14 healty volunteers, FEV_1, VC, DLco, D_M were impaired in CHF and did not improve with carvedilol. It significantly reduced LVEDP, EDD, ESD, and increased SV, EF, Vcf but failed to ameliorate pVO_2, VO_2at, pVD/VT, VE/VCO_2. Placebo was not effective. Data at 3 and 6 months were similar.

Conclusions: Lack of pulmonary function improvement despite excellent amelioration of left ventricular function, suggests the development in CHF of an irreversible or slow reversible organic lung disease, or a need for pharmacological properties that carvedilol does not possess. Persistent pulmonary dysfunction may prevent pVO_2 improvement.

1015-32 Long-term Survival Effect of Metoprolol in Dilated Cardiomiopathy

A. Di Lenarda, R. De Maria, A. Gavazzi, D. Gregori, M. Parolini, G. Sinagra, L. Salvatore, F. Longaro, E. Bernobich, F. Camerini. *Department of Cardiology, Trieste; Istituto di Fisiologia Clinica CNR, Milano, Italy*

Background: Although metoprolol (M) is effective in dilated cardiomyopathy (IDC), controlled data are lacking on long term survival. We evaluated the effect of M on long-term survival in 586 pts with IDC, prospectively enrolled in a multicenter registry and followed up for 52 ± 32 months. M, uptitrated to the maximum tolerated dose, was added to conventional therapy in 175 of them.

Results: Seven-year survival (81% *vs* 60%, p = 0.0001) and transplant-free survival (69% vs 49%, p = 0.0004) were higher in the 175 M-treated pts than in the 411 on standard treatment. By multivariate analysis, M was associated to a 51% reduction for all-cause mortality (95% CI −21 to −69%, p = 0.002) and a 34% for mortality or transplantation (95% CI −5 to −53%, p = 0.01). NYHA class, LV end diastolic diameter and pulmonary wedge pressure were likewise predictive. Seven-year survival (80% *v* 62%, p = 0.0036) and transplant-free survival (68% *v* 51%, p = 0.0053) were also higher in 127 M-treated cases than in 127 controls, appropriately matched for key prognostic variables. M pts showed a 30% reduction in all-cause mortality (95% CI −7% to −48%, p = 0.0147) and a 26% reduction in mortality or transplantation (95% CI −7% to −41%, p = 0.0009).

Conclusions: The addition of metoprolol to standard therapy, including ACE-inhibitors, was effective in the long-term, reducing both all cause mortality and transplantation in patients with IDC.

1015-33 Beta-Blocker Therapy in Patients With Clinical Evidence of Heart Failure After Acute Myocardial Infarction

C.S. Spargias, A.S. Hall, S.G. Ball. *Institute for Cardiovascular Research, University of Leeds, UK*

Background: Clinical evidence of congestive heart failure (HF) after acute myocardial infarction (MI) is considered by many to be a contraindication to β-adrenergic blockade. Furthermore, there is uncertainty as to the value of these agents following routine use of aspirin, thrombolytic and ACE-inhibitor therapy. We examine clinical outcomes associated with optional β-blockade in a post MI population with evidence of HF.

Methods: We retrospectively analyzed data from the AIRE study (randomized, placebo-controlled trial of ramipril in 2006 post MI patients with clinical evidence of HF). At baseline, 20% of the patients were receiving a β-blocker. Diuretic treatment at randomization defined a high risk group with poorer left ventricular function (LVF). To eliminate confounding, we separately analyzed patients according to diuretic use, adjusting for the presence of multiple clinical signs of HF and 15 other baseline clinical variables. Each was simultaneously entered in a multivariate Cox regression model.

Results: β-blocker therapy was a significant independent predictor of reduction in the risk of all-cause mortality (34%, CI 10% to 51%, p = 0.008) and severe HF (43%, CI 18 to 60%, p = 0.002) for the entire study population. Similar findings occurred in high risk patients receiving diuretic (39%, CI 10% to 58%, p = 0.012; 42%, CI 11% to 62%, p = 0.013) but not in those not requiring diuretic use (19%, CI −38 to 53%, NS; 41%, CI −17% to 70%, NS).

Conclusion: Our data indicate that in the modern era β-blocker therapy benefits patients with clinical evidence of HF post MI.

1015-34 Evidence Against Heart Rate Reduction as the Primary Mechanism of Action of Carvedilol in Chronic Heart Failure

J.D. Sackner-Bernstein, M.A. Lukas, B. Wu. *For the U.S. Carvedilol Investigators; Columbia University, College of Physicians & Surgeons New York, USA*

Carvedilol (CV) reduces morbidity and mortality and improves quality of life in patients with heart failure (HF). A mechanistic role of heart rate reduction (ΔHR) has been postulated. We evaluated the relationships between the ΔHR by CV and its long-term clinical and left ventricular effects.

Patients enrolled in the US trials who received carvedilol for their double-blind therapy were evaluated (n = 696). Most had NYHA II–III symptoms, and mean ejection fraction (EF) was 0.23. CV was started at 6.25 mg BID and titrated to 25–50 mg BID over 4–6 weeks. ΔHR was calculated from the difference between heart rates prior to and after titration. Logistic regression was performed to determine if ΔHR was related to 1) progression of HF, 2) global assessment by physician and patient, 3) ΔNYHA class, 4) Δsymptom status, and 5) ΔEF. Patients were divided by the median ΔHR with comparison of outcome variable.

ΔHR correlated significantly but weakly with ΔNYHA and ΔEF (r = 0.08, p = 0.03 and r = 0.15, p = 0.003, respectively). Patients with the greatest ΔHR did not have a different clinical outcome.

ΔHR does not correlate strongly with the long-term effects of CV. Neurohormonal antagonism independent of chronotropic effects may be the primary mechanism of benefit. The degree of ΔHR should not be the clinical target when treating patients with carvedilol.

1015-35 Effect of Carvedilol on Symptom Score in Heart Failure

E.M. Gilbert, M.A. Lukas, B. Wu, M.B. Fowler. *For the US Carvedilol Heart Failure Study Group; University of Utah, Salt Lake City, UT, USA*

Patients (pts) in the US Carvedilol (C) Heart Failure (HF) Trials Program randomized to placebo (P, n = 398) or C (n = 696) had HF symptoms assessed by a quantitative score of fatigue and of dyspnea (rest, walking on level ground and climbing stairs) by a scale of 0 (none) to 3 (severe). Pts' well-being was rated by a scale of 0 (very good) to 3 (poor). Maximum possible overall score was 0–21.

Results: Table of within and between group (P vs C) changes at endpoint: Analyzed by baseline severity (submaximal exercise intolerance), overall score improved on C vs P by 1.3 (p < 0.01). 0.5, and 1.8 (p = 0.10) in pts with mild, moderate or severe impairment, respectively.

Question	BL	ΔP	BL	ΔC	ΔP vs C
Overall	8.4	−0.63	8.3	1.27	0.64*
Dyspnea-rest	0.5	0.04	0.5	0.04	0.08**
Dyspnea-level	1.1	−0.15	1.1	−0.17	0.02
Dyspnea-stairs	1.7	−0.18	1.7	−0.24	0.06
Fatigue-rest	0.8	−0.07	0.8	−0.11	0.04
Fatigue-level	1.1	−0.02	1.1	−0.18	0.16*
Fatigue-stairs	1.6	−0.09	1.7	−0.27	0.18†
Pts well-being	1.5	−0.17	1.5	−0.26	0.09‡

* p = 0.01; ** p = 0.08; † p = 0.003; ‡ p = 0.09 [BL = baseline].

Conclusion: Analyzed using a quantitative heart failure symptom score, carvedilol treatment was associated with significant improvements in overall score, and in exertional fatigue, with evidence for benefit regardless of baseline severity.

1015-36 Contrasting Effects of Intravenous Dofetilide and Amiodarone on Cardiac Sympathetic Drive in Patients With Congestive Heart Failure

M.F. Rousseau, P.E. Massart, L. Galanti, S.A. Ahn, J. Etienne, H.G. Pouleur. *University of Louvain, Brussels, Belgium*

In contrast to IV dofetilide (DOF, a pure IKr blocker), IV amiodarone (AMIO) lowers aortic pressure and hence, could trigger baroreceptor reflex. To assess the implications of this systemic effect of AMIO at the cardiac level, coronary sinus (CS) flow (thermodilution) and aortic and CS norepinephrine (NE) concentrations were measured in 30 pts with congestive heart failure (NYHA II–III; LVEF: 19 ± 8%), before and after a 30 min infusion of placebo (P; n = 12), DOF (8 μg/kg; n = 12) or AMIO (5 mg/kg; n = 6). CS flow was little affected by infusions (P: +3.6%; DOF: −4.0%; AMIO: +4.7%; all NS) and myocardial O2 consumption decreased slightly with all drugs (P: −1.0 ml/min; AMIO: −0.2; DOF: −1.6; all NS). AMIO alone significantly decreased dP/dt Max and mean aortic P (−9 $mmHg^{*\delta}$) whereas only DOF prolonged single lead QT (+106 $ms^{*\delta}$ vs +10 with AMIO and +9 with P). However, AMIO increased